EFFECT OF α_1-ADRENORECEPTOR BLOCKADE ON STRUCTURE AND FUNCTION OF THE RENAL ENDOCRINE SYSTEM

B. N. Salikhov

UDC 612.46:576.8.097.1+615.217.24

KEY WORDS: kidney; juxtaglomerular cells; interstitial cells; α_1-adrenoblockers.

Adrenoreceptors of various subtypes are mediators of renal functional responses to changes in activity in the renal nerves and in the concentration of circulating catecholamines. Meanwhile there is sporadic and contradictory information on the role of α_1-adrenoreceptors in functioning of the renal endocrine system [4-6]. Results obtained on slices of renal blood vessels in vitro and in investigations on isolated, perfused kidneys, indicate that α_1-adrenoreceptor activation inhibits renin secretion. However, the results of a study of the role of α_1-adrenoreceptors in the regulation of renin secretion in vivo were contradictory [4]. Some workers [6, 7] consider that α_1-adrenoreceptors are involved in renal release, when renal hemodynamic changes are present and the blood flow in the kidneys is slowed. Thus the available data on the influence of α_1-adrenoreceptors on renin secretion in vitro and in vivo are contradictory and do not explain the decrease in the renal blood flow in response to their activation [8]. We have no information on the role of α_1-adrenoreceptors in prostaglandin secretion by the interstitial cells of the kidneys.

The aim of the investigation described below was accordingly to study structural and functional aspects of the juxtaglomerular and interstitial cells of the kidneys during acute and chronic α_1-adrenoreceptor blockade.

EXPERIMENTAL METHOD

The test objects were 30 noninbred male albino rats weighing 140-150 g. All the animals were divided into five experimental groups. Group 1 (n = 6) served as the control; group 2 (n = 6) received the α_1-adrenoblocker adversuten in a single dose of 0.5 mg/kg body weight; group 3 (n = 6) received the same dose of adversuten 3 times a day for 30 days; group 4 (n = 6) received prazosin (a Soviet α_1-adrenoblocker) in a single dose of 0.5 mg/kg body weight; group 5 (n = 6) received prazocin in the same dose 3 times a day for 30 days. The animals were killed 90 min after injection of the drug. Pieces of kidney tissue taken from the cortical and intramedullary zones of the kidneys were fixed in a 1% solution of glutaric acid, made up in 0.1 M phosphate buffer, pH 7.4, and postfixed in 1% OsO_4, made up in phosphate buffer with sucrose. The tissue was then dehydrated in alcohols and acetone and embedded in Araldite. Ultrathin sections were cut on the LKB 4800 Ultramicrotome, stained by Reynolds' method, and examined in JEM-100B and JEM-100S electron microscopes.

EXPERIMENTAL RESULTS

The electron-microscopic investigations of the kidneys of rats receiving both adversuten and prazasin revealed consistent changes, which did not differ significantly in the two cases.

In the juxtaglomerular complex, after a single dose of the α_1-adrenoblockers secretory activity was depressed, as shown by reduction of the rough endoplasmic reticulum and of elements of the Golgi lamellar complex. Against this background, many homogeneous secretory granules, with high electron density, were found in the cytoplasm of the juxtaglomerular cells (Fig. 1a).

Research Institute of Cardiology, Ministry of Health of the Uzbek SSR. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 113, No. 2, pp. 211-214, February, 1992. Original article submitted April 19, 1991.

0007-4888/92/0002-0281$12.50

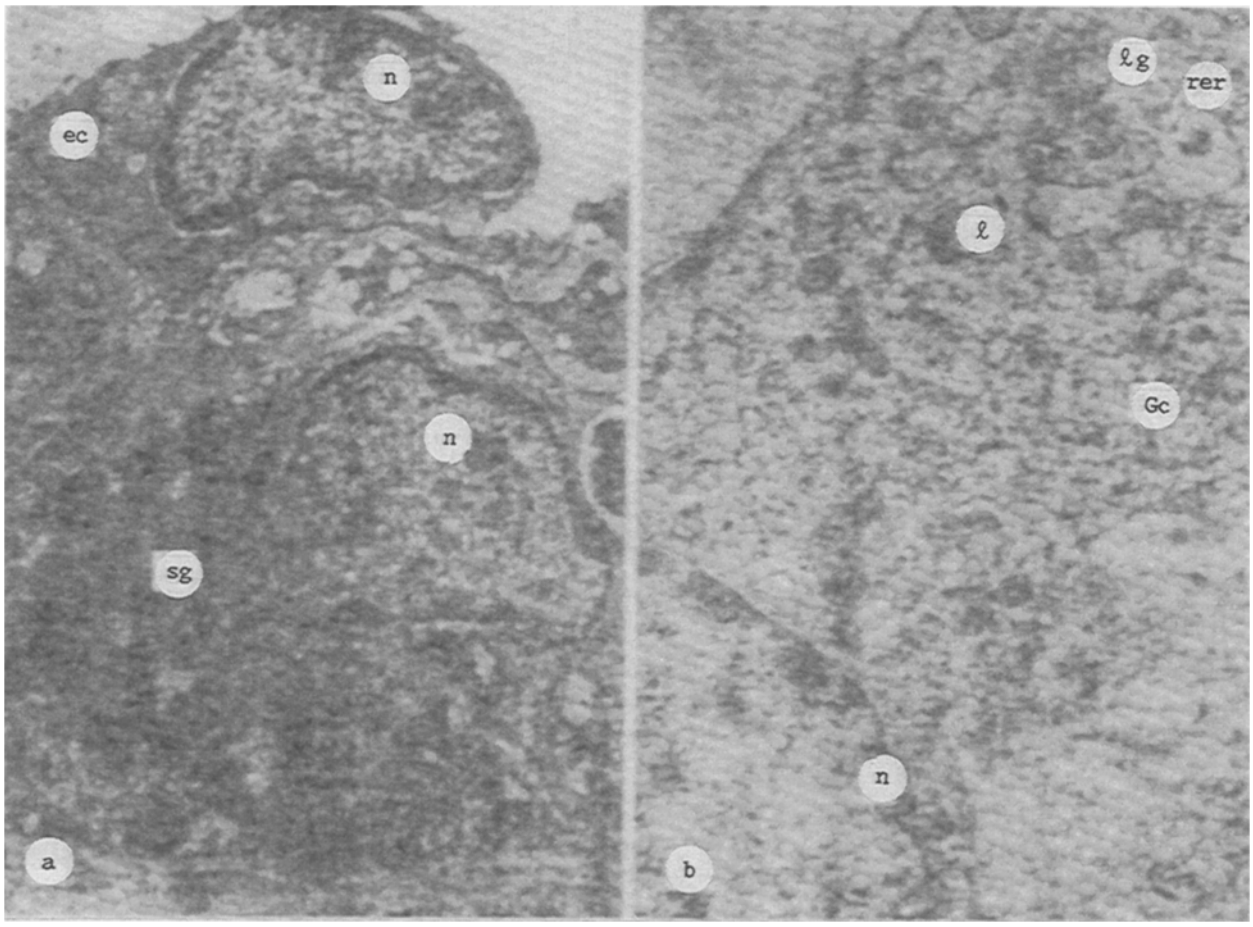

Fig. 1. Morphologic features of juxtaglomerular and interstitial cells after administration of a single dose of α_1-adrenoblockers: a) juxtaglomerular cell; b) interstitial cell; n) nucleus, sg) secretory granules; *lg*) lipid granules, *l*) lysosomes, Gc) Golgi complex, rer) rough endoplasmic reticulum; ec) endothelial cell. 25,000×.

A single injection of the α_1-adrenoblockers is accompanied by a hypergranular form of depression of juxtaglomerular cell function. This form of hypofunction of the renin-secreting structures, incidentally, arises when the release of secretion, its accumulation, and the secondary inhibition of its synthesis by the feedback principle are depressed [1, 2].

Against the background of the changes in the juxtaglomerular complex described above the following changes were found in the interstitial cells of the inner medullary layer of the kidneys. The interstitial cells contained a hypertrophied rough endoplasmic reticulum and a strongly developed Golgi lamellar complex in their cytoplasm. The Golgi complex consisted mainly of vesicles. The number of lipid granules in the cytoplasm was reduced. Against this background of the state of the intercellular structures, various kinds of electron-dense lysosomes appeared in large numbers (Fig. 1b).

The predominant interstitial cells were those with the ultrastructure described above. This type of ultrastructure is characteristic of cells whose functional state is activated, i.e., prostaglandin synthesis is increased [3].

Thus after a single injection of α_1-adrenoblockers there was a simultaneous decrease in functional activity of the juxtaglomerular cells and an increase in the prostaglandin-synthesizing function of the interstitial cells of the inner medullary layer of the kidneys.

Long-term (30 days) administration of the α_1-adrenoblockers also was accompanied by changes of the same type in response to prazosin and adversuten. The juxtaglomerular cells in this case were somewhat reduced in size. They contained a relatively large nucleus with a narrow border of cytoplasm (Fig. 2).

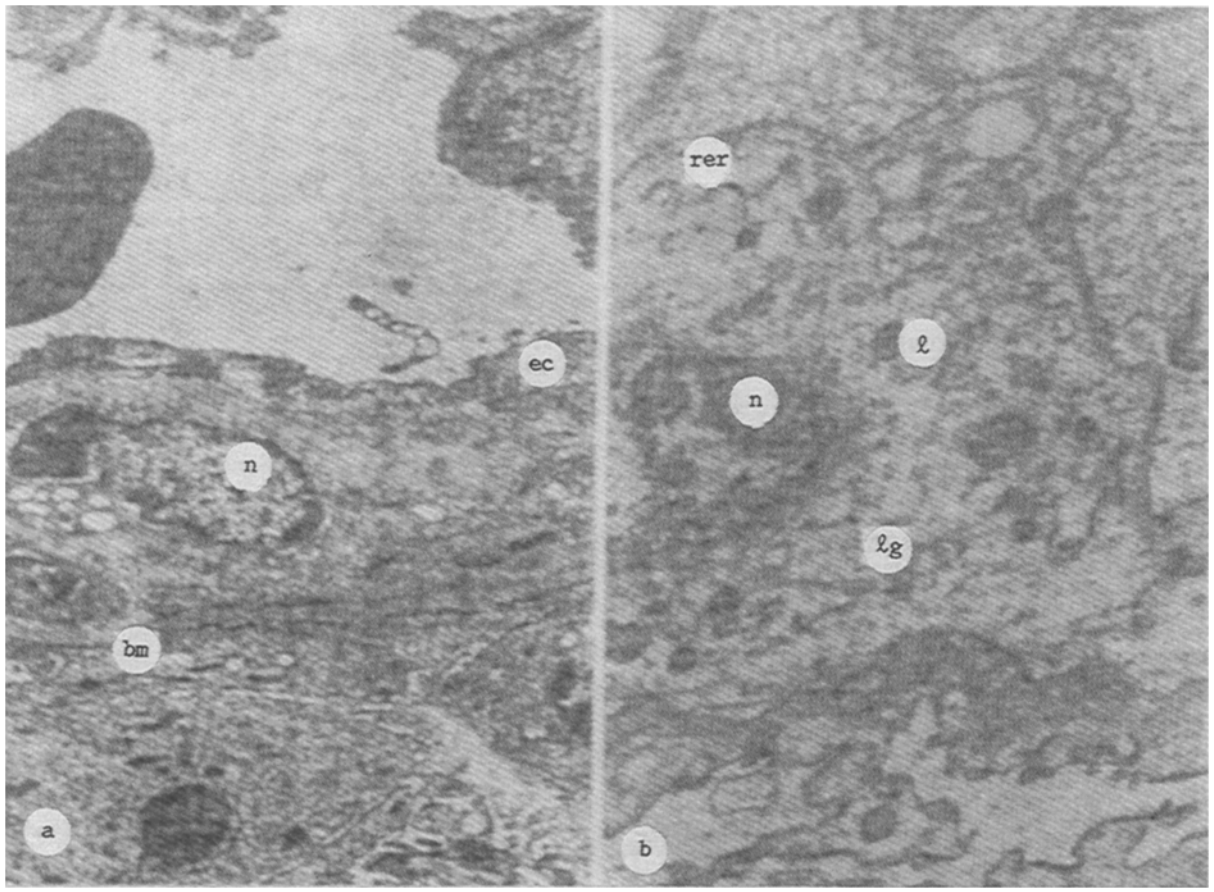

Fig. 2. Morphologic features of juxtaglomerular and interstitial cells in response to long-term administration of α_1-adrenoblockers. bm) Basement membrane. Remainder of legend as to Fig. 1. 25,000×.

Numerous free ribosomes and polysomes were found in the cytoplasm. There was a sharp decrease in the number of the other organelles, particularly of the rough endoplasmic reticulum. No secretory granules were found in the cytoplasm. Degranulation of the juxtaglomerular cells, against the background of a decrease in the number of their protein-synthesizing structures, points to depression of renin synthesis [1, 2].

Most of the interstitial cells of the inner medullary substance of the kidneys preserved their functionally active state, characterized by hypertrophy of the rough endoplasmic reticulum and lamellar complex, and by a larger number of lysosomes than of lipid granules.

Long-term administration of the α_1-adrenoblockers led to reduced functional activity of the juxtaglomerular complex and activation of prostaglandin synthesis by the interstitial cells of the inner medullary substance of the kidneys.

Thus a single injection of the α_1-adrenoblockers was accompanied by a decrease in renin release and simultaneous activation of prostaglandin production by the interstitial cells. In the case of long-term administration (for 30 days) of the α_1-adrenoblockers, the state of blocking of renin release by the juxtaglomerular cells persisted, and led to a decrease in renin secretion by the feedback principle, with a decrease in the number of protein-synthesizing structures. Under these circumstances functional activation of the intracellular structures of the interstitial cells responsible for prostaglandin synthesis took place.

LITERATURE CITED

1. V. M. Gontmakher, "Functional morphology of the kidney and its particular features in postnatal ontogeny," Dissertation for the Degree of Doctor of Medical Sciences, Tashkent (1978).

2. K. A. Zufarov, V. M. Gontmakher, and B. A. Khidoyatov, Cytofunctional Aspects of the Kidney [in Russian], Tashkent (1974).
3. K. A. Zufarov, V. M. Gontmakher, and A. A. Khamraev, Arkh. Patol., **49**, No. 1, 9 (1987).
4. T. A. Kotchen and M. W. Roy, in: M. J. Dunn (ed.), The Renin-Angiotensin System [Russian translation], Moscow (1987), pp. 241-272.
5. M. L. Blaiz, Am. J. Physiol., **244**, 37 (1983).
6. M. L. Blaiz and Y. H. Chen, Am. J. Physiol., **248**, 317 (1985).
7. G. F. Di Bona, J. Cardiovasc. Pharmacol., No. 7, Suppl. 8, 18 (1985).
8. J. Hiroshi, J. Jadoshimo, and S. Osamu, Stroke, No. 3, 629 (1987).